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CHANGES IN TISSUE VULNERABILITY INDUCED DURING HYPNOTIC SUGGESTION*†

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GRAHAM (1950) studying patients with urticaria about 10 years ago in the laboratories of the New York Hospital, showed that the tone of the minute vessels in the skin was reduced and permeability increased in situations perceived as threatening or during the discussion of them. Under these circumstances heretofore non-noxious stimuli, both mechanical and chemical, became capable of inducing flush, itching and urticaria and in some instances these latter phenomena occurred spontaneously.

Although careful descriptions of methods and results are rare, it has long been alleged that lesions in the skin could be induced by suggestion during hypnosis. A recent and well documented instance is that of ULLMAN who induced erythema with blister formation that was noted at the end of an hour, and was fully developed approximately 4 hr later (ULLMAN, 1947).

In this laboratory also it has been possible in experiments during hypnosis to demonstrate the occurrence of erythema and whealing in response to repeated suggestions that a warm rod applied to the skin was hot and would burn the skin (CHAPMAN *et al.*, 1959a). This observation was further evidence that activities at the highest integrative levels of the nervous system could modify the magnitude of inflammatory reactions in the periphery. In the studies reported in this communication experiments were designed to demonstrate that the degree of inflammatory response and tissue damage to a standard noxious stimulation could be augmented or diminished by activity of the central nervous system integrated at the highest levels. As an aid in manipulating these activities by the suggestion of relevant symbols the hypnotic state was induced. It was, however, recognized that the hypnotic state, *per se*, is not essential to the effects associated with suggestion, symbols and memories.

METHOD

Thirteen adult men and women served as subjects. Three of these were patients who had spontaneously occurring urticaria. The remainder were healthy and free of skin disorders.

Experiments were conducted in a quiet, semi-darkened, comfortably cool room. Thermocouples were attached to the subject's arms and a series of control temperatures recorded by means of a multichannel recording instrument. Finger cuffs for recording of the plethysmograms, were attached to the middle finger of each hand and control recordings made.

The subjects were hypnotized in the conventional manner. As soon as a state of moderate to deep hypnosis had been established it was suggested that one arm was either 'normal', or that it was 'numb', 'wooden' and devoid of sensation ('anaesthetic'). It was then suggested that the other arm was painful, burning, damaged and exceedingly sensitive, i.e., 'vulnerable'. Furthermore, it was suggested

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that severe injury to this 'vulnerable' arm which would cause even greater pain and damage was about to occur. The 'vulnerable' arm was then exposed on three spots blackened with India ink, to standard noxious stimulation (500 mcal-cm²-sec for 3 sec). After an interval of 15–30 min during which hypnosis was continued, suggestions that the other arm was either 'anaesthetic', or 'normal' were repeated and reinforced. It was then similarly exposed on three spots to the standard noxious stimulation. In some experiments the order of exposing the 'vulnerable' or 'anaesthetic' arm to noxious stimulation was reversed. Also, the right arm was suggested to be 'vulnerable' in some experiments, the left in others. In some experiments the suggestion of 'vulnerability' for one arm and 'anaesthesia' for the other were made simultaneously and the noxious stimulation was applied during the same interval alternately on the two arms.

The inflammatory reaction and tissue damage were assessed by observations and measurements of area, intensity and duration of erythema, oedema, blister formation, necrosis and when present, of residual scar formation. Coloured photographs were made approximately 20 min after the end of an experiment, and at 24 hr intervals for about 2 weeks.

In one subject the subcutaneous spaces in the zones of axon reflex flares induced by the noxious stimulation were perfused. The method of perfusing the subcutaneous space is a modification of that of FOX and HILTON (1958) and for obtaining fluid inflow and outflow perforate needles were used. These needles were #20 steel hypodermic needles with eight perforations in the shafts.* The needles were inserted into the subcutaneous space of the volar surface of the forearm parallel to each other and approximately 1·5 cm apart. The rate of inflow of the perfusion fluid (physiological saline) was 0·5 ml/min. Six minute samples of the perfusate were collected throughout the experiment during 30–60 min thereafter. The perfusate was collected in siliconized tubes and was immediately assayed or frozen in solid CO_2 to prevent alteration and then subsequently assayed when convenient. The perfusates were assayed by the conventional smooth muscle (rat uterus and duodenum) methods. After the desired suggestions of 'vulnerability' in one arm and 'anaesthesia' in the other were made, the skin of the two arms was injured by standard noxious thermal stimuli at a distance of approximately 4 cm on either side of the collection site. Aliquots (0·2 ml) of the samples of perfusate were added to the chamber containing the muscle strip and the amplitude of contractions induced expressed as the amount of bradykinin standard required to induce similar contractions.

RESULTS

The thirteen subjects were hypnotized in 40 experiments. During 12 of these, increased pain and damage were suggested in one arm, and on the opposite side suggestions that the arm was normally sensitive were made. The inflammatory reaction and tissue damage was greater on the side of suggested 'vulnerability' in 9 of this series of 12 experiments; in 1 increased damage was observed on the side of suggested normal sensitivity and in 2 no difference was noted. In 27 experiments it was suggested that one arm was 'vulnerable' and that the other arm was 'anaesthetic'. In 1 experiment greater damage occurred in the arm of suggested 'anaesthesia'. In 6 no difference was observed in the two arms. However, in 20 of this series of 27 experiments the inflammatory reaction was greater on the side of suggested pain and damage. In 1 experiment it was suggested that one arm was anaesthetic, the other normally sensitive. The reaction was far greater on the normal side. Although the

* The perforated needles were specially made by Becton Dickinson Co.

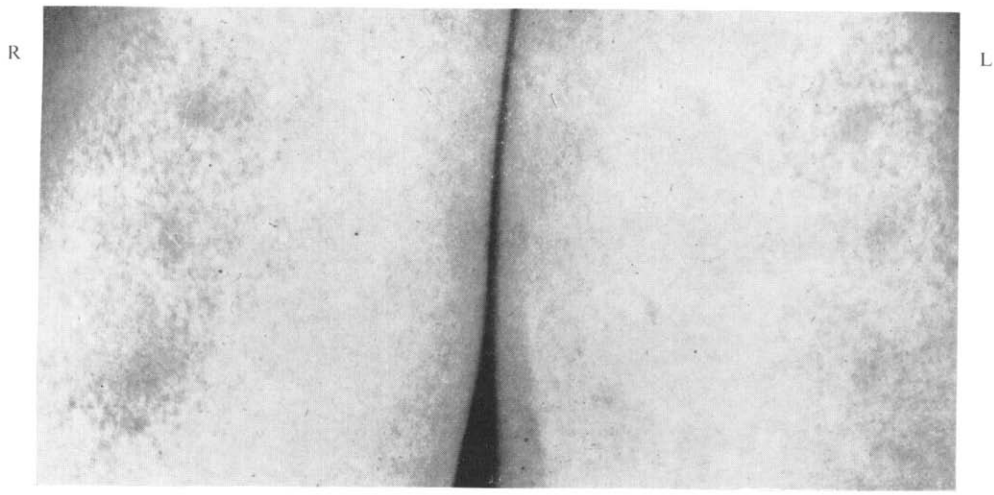

FIG. 1.—Photograph of the arms of subject L. O. made approximately ½ hr after noxious thermal stimulation during hypnosis. The right arm was suggested to be 'vulnerable', the left arm 'anaesthetic'. The burns were made in quick alternation from one arm to the other within a period of 30 sec. Note the more extensive erythematous reaction surrounding the burns on the 'vulnerable' arm (right).

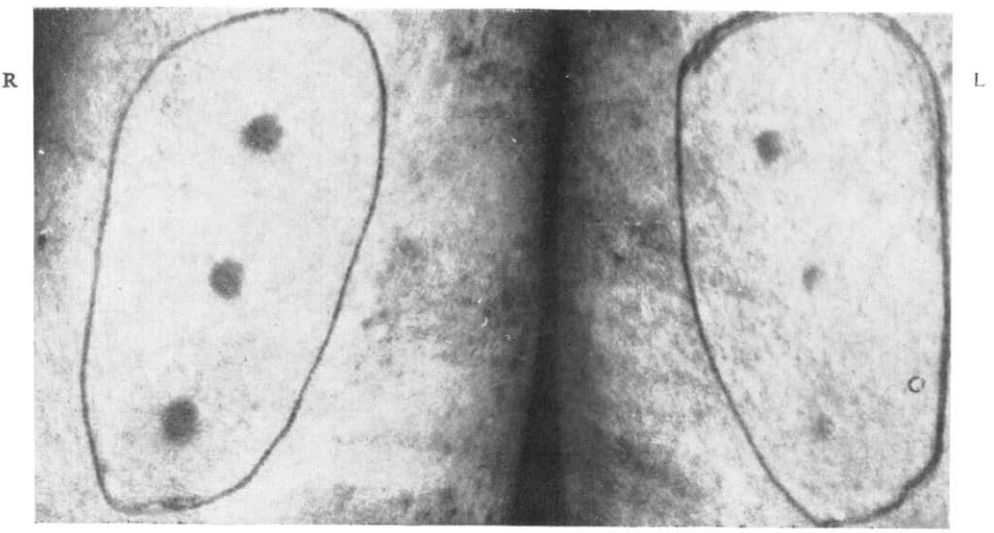

FIG. 2.—The arms of subject L. O. photographed 4 days later than the photographs of Fig. 1. Note the greater tissue damage on the 'vulnerable' right arm, as compared with that on the anaesthetic' left arm, resulting from identical intensities and durations of noxious thermal stimulation.

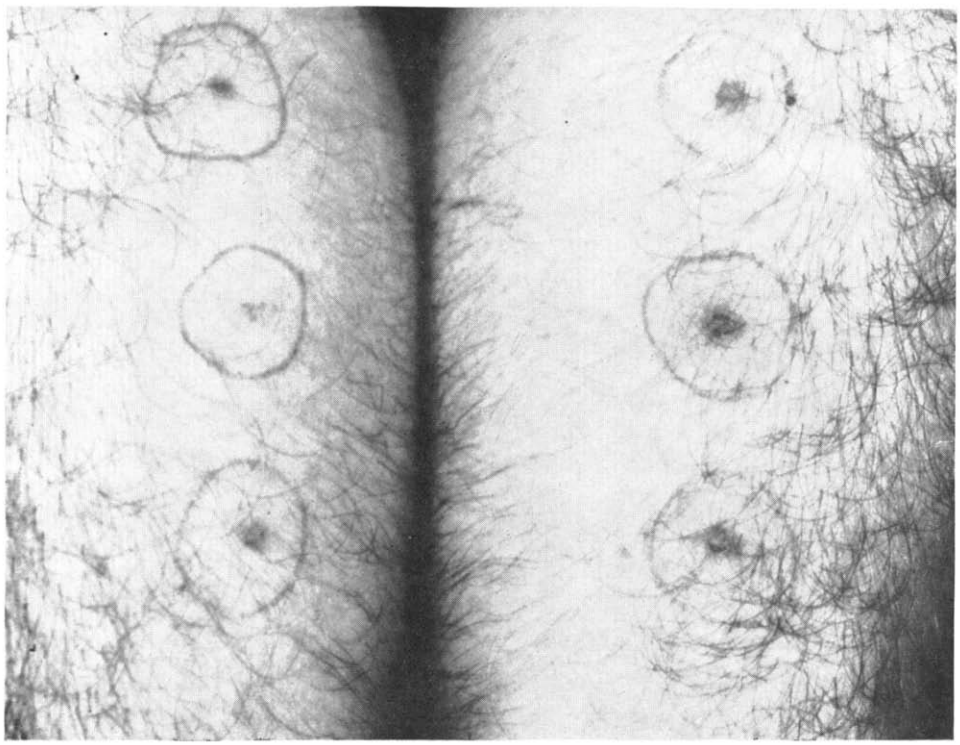

FIG. 3.—Photograph of the arms of subject S. H. made 3 days after noxious thermal stimulation during hypnosis. The burns were made in quick alternation from one arm to the other while the left was being suggested as 'vulnerable', the right arm as 'anaesthetic'.

contrast was greatest in the magnitude of reaction between suggested 'anaesthesia' and suggested 'vulnerability', it was also evident that the effect of suggested 'anaesthesia' was to suppress the inflammatory reaction as contrasted with no suggestion or suggestion of normality.

In Figs. 1–3 are shown the greater damage in the vulnerable arms, and the lesser damage in the 'anaesthetic' arms after identical thermal stimulation of the two limbs. One patient who complained of spontaneously occurring urticaria developed urticarial

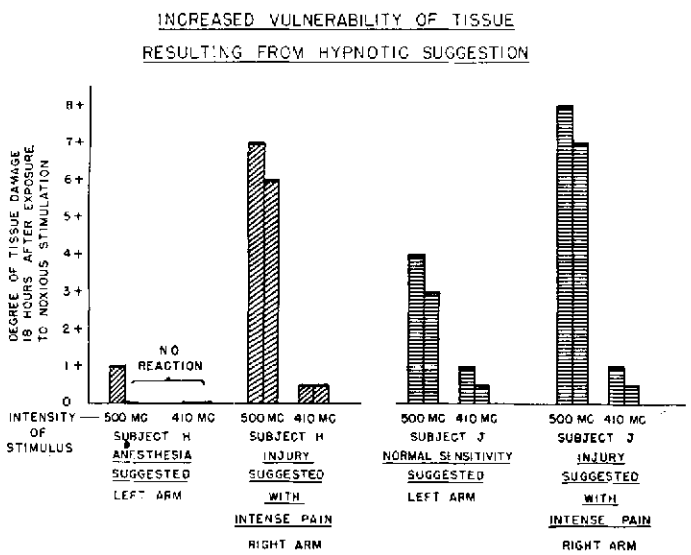

FIG. 4.—Diagramatic representation of increased vulnerability of tissue induced during hypnotic suggestion in two subjects, 'H' and 'J'. Two intensities of thermal stimulation were used, and the effects of suggested anaesthesia compared with those of 'vulnerability' in subject 'H'; and the effects of suggested normal sensitivity compared with those of 'vulnerability' in subject 'J'.

reactions in other parts of her 'vulnerable' arm following noxious stimulation by heat (500 mcal-cm^{-2}-sec^{-1} for 3 sec). Urticaria was not observed on the 'anaesthetic' arm at this time.

In two experiments in two subjects two exposures of 500 mcal and two exposures of 410 mcal were made on each arm. The less intense stimulation was used in order to ascertain whether the effects of highest level functions would be more conspicuous when the damaging stimulus was less intense. It was shown that when anaesthesia was suggested in the one subject no visible damage could be perceived 18 hr after the stimulation with 410 mcal, whereas when injury with intense pain was suggested this less intense stimulus produced a readily detectable lesion.

In the second subject the difference in reaction between the arm with normal sensitivity and the one with suggested injury and intense pain was less striking but the inflammatory response to the more intense stimulation was conspicuous (see Fig. 4), on the side of suggested 'vulnerability'.

Experiments designed to ascertain the nature of the relevant tissue responses that could explain the greater amount of damage in the 'vulnerable' arms were then carried out. The two arms were prepared for measurement of skin temperature, for finger plethysmographic recordings and for the collection of perfusate. These

observations were made before and during the period of hypnosis, both before and after the application of noxious stimuli. No significant differences in the amplitude of finger pulsations, in the skin temperature of the arms, or in the bradykinin content as measured in the perfusates could be observed between the 'anaesthetic' and the 'vulnerable' arms before the damaging stimulus was applied, although other experiments in this laboratory indicate that such differences may be induced during suggestion alone. Under the given experimental circumstances reported here, in response

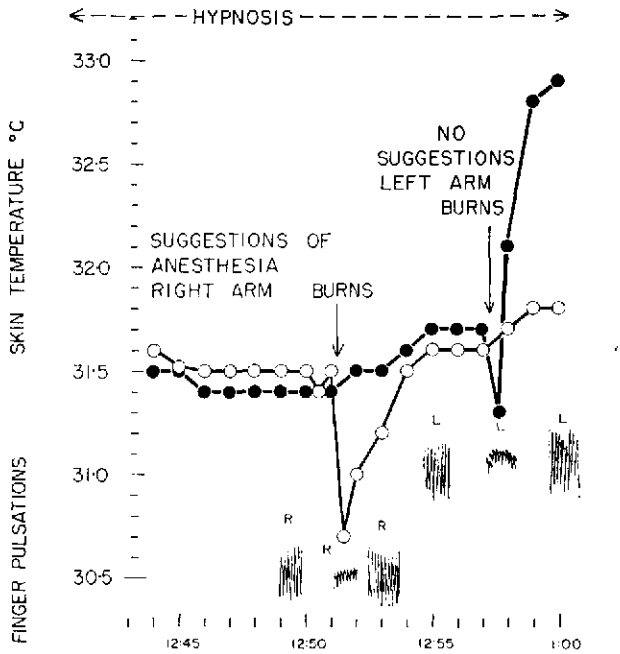

FIG. 5.—Measurements during hypnosis of the skin temperature and amplitude of finger pulsations of the right 'anaesthetic' arm and of the left arm stated to be normally sensitive. Note the larger initial vasoconstriction as indicated by fall in skin temperature in the arm suggested to be anaesthetic (right), and the markedly reduced subsequent vasodilatation as compared to the reaction to the burns on the normally sensitive side (left). The absence of, or the minimal vasodilatation after injury in the arm suggested to be 'anaesthetic' affords a partial explanation of the minimal effect of injury.

to noxious stimulation there was a greater and longer sustained rise in the skin temperature of the 'vulnerable' arm (Figs. 5 and 6) as well as a greater increase of bradykinin content in the perfusate from this arm (Fig. 7) as compared with the 'anaesthetic' arm. The greater rise in skin temperature occurred in all experiments in which damage was greater on the 'vulnerable' arm. A corresponding increase in finger pulsations was frequently seen, but was less predictable.

COMMENT

Experiments with immersion in hot water, (BILISOLY *et al.*, 1954) implicating the thermoregulatory centres in the brain stem and hypothalamus and experiments with hypnosis, implicating the highest levels of neural integration, demonstrated that activity within the central nervous system at several levels can augment the effects of the axon reflex (CHAPMAN *et al.*, 1959b). The occurrence of spontaneous urticaria

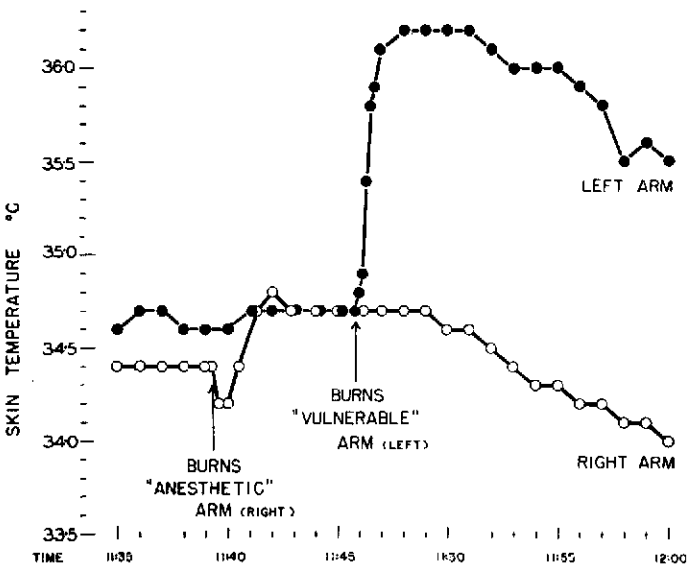

FIG. 6.—Measurements during hypnosis of the skin temperature of the right ('anaesthetic') and the left ('vulnerable') arm previous to, during, and following the application of a damaging heat stimulus (500 mcal-cm^{-2}-sec^{-1} for 3 sec). The right arm was suggested to be numb, anaesthetic and without feeling, whereas the left arm was suggested to be already damaged, painful and about to be injured further. Note the greater degree and more persistent rise of skin temperature after suggestion of damage, indicating the pertinence of vasodilatation to the enhanced inflammatory reaction to injury.

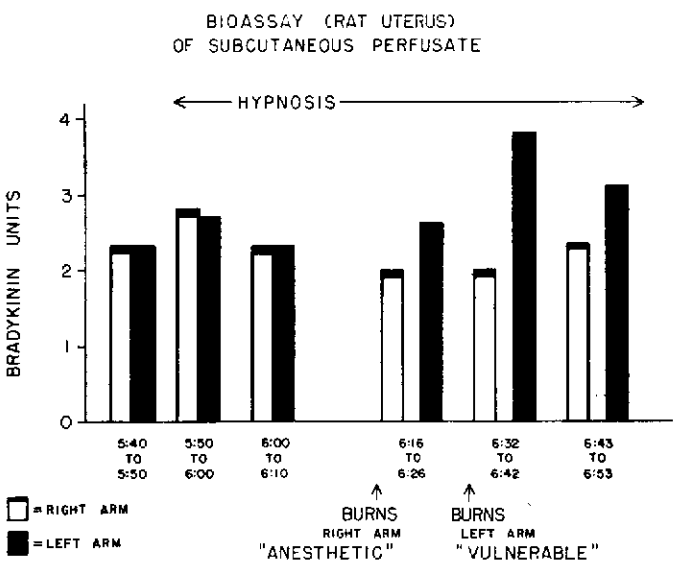

FIG. 7.—Bioassay of the subcutaneous perfusate expressed as units of a standard preparation of bradykinin inducing equivalent contractions of the rat uterus. After injury of the 'vulnerable' arm during hypnosis there was more bradykinin activity in the perfusate from the flare zones induced by the thermal injury than in the perfusate from the arm suggested to be 'anaesthetic'.

observed in one susceptible subject in this study suggests a widespread heightened reactivity in the vulnerable arm during the threatening situation created by suggestion and by burns.

It thus appears that the individual's perceptions and attitudes are relevant to neural activities that engender or enhance inflammatory reactions. The liberation or accumulation of proteolytic enzymes in the periphery and the subsequent formation of a bradykinin-like humoral agent is implicated in these heightened reactions.

Enhanced inflammation has been shown to be effective in combating invasion by micro-organisms and in the rapid elimination of tissue breakdown products of injury. Therefore, the present alternations indicate that man includes among his adaptive and protective devices, neural reactions integrated at the highest levels that heighten inflammation in the peripheral tissues and increase the local susceptibility to injury—thus enhancing the protection of the whole organism at the cost of the integrity of a part. Such adaptive reactions at times may be essential to survival, but if evoked inappropriately or excessively may contribute to disease since non-noxious stimulation becomes noxious and mildly damaging stimuli result in greater injury. On the other hand, the observations reported here clearly suggest that activity of the highest integrative functions may also prevent excessive or inappropriate response and initiate appropriate tissue reactions.

SUMMARY AND CONCLUSIONS

(1) Following standard amounts of noxious stimulation on the forearm during hypnosis, decreased inflammatory reaction and tissue damage was observed when the suggestion was made that the arm was insensitive and numb and would not be hurt, 'anaesthetic', as compared to the reaction and tissue damage of the other arm which was suggested to be normally sensitive.

(2) Following standard amounts of noxious stimulation on the forearm during hypnosis, increased inflammatory reaction and tissue damage was observed in subjects who had received the suggestion that the forearm was tender, painful and injured ('vulnerable') as compared with arms suggested to be normally sensitive or 'anaesthetic'. Recordings of finger pulse amplitude and skin temperature indicated that local vasodilatation following exposure to noxious stimulation was larger in magnitude, and persisted longer in the 'vulnerable' arm. The subcutaneous perfusate from the arm suggested to be painful, tender and damaged developed a greater increase of a pharmodynamic substance in response to standard noxious stimulation than did that from the arm suggested to be 'anaesthetic'.

(3) This pharmocodynamically active substance induced itching, local vasodilatation and oedema, lowered blood pressure, lowered pain threshold, induced delayed and slow contraction of the rat uterus and guinea pig ileum and resulted in relaxation of the rat duodenum. It deteriorated at room temperatures, was stabilized by boiling and destroyed by chymotrypsin. It was not acetylcholine, histamine or serotonin, although these and other relevant agents may also have been present. It had many of the properties of a polypeptide of the bradykinin type.

(4) Neural activity involving the segmental or axon levels, the brain stem and hypothalamic levels, as well as the subcortical and cortical levels can alter the reactions in the peripheral tissues subserved in such a way as to augment inflammation and increase local tissue damage in reaction to noxious stimulation. Proteolytic enzymes and a bradykinin-like polypeptide is implicated in these enhanced reactions.

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